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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SODERQUIST, ARLEN	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,419	MALIK ET AL.	
	Examiner	Art Unit	
	Arlen Soderquist	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-13-05,6-24-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 13, 2005 has been entered.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 21-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Examiner cannot find any basis in the specification for specifically excluding a cross-linked organic ligand. For examination purposes this limitation will be treated as limiting and as non-limiting. In fact page 18 of the instant specification teaches Ucon is a polyethylene glycol that is usable in the instant invention (see page 22 for its use). This is what is "cross-linked" in the Hayes reference. Furthermore the cross-linking reaction can occur through a number of mechanisms: gamma irradiation (see US 4,509,964), plasma treatment (see US 4,966,785) and various cross-linking agents.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 21-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes (1997, hereinafter called Hayes '97) in view of Ogden or Sumpter and optionally Hayes (1996, hereinafter called Hayes '96) and Wang. The Hayes '97 reference teaches sol-gel chemistry-based Ucon-coated columns for capillary electrophoresis. A sol-gel chemistry-based novel approach for the preparation of a Ucon-coated fused-silica capillary column in capillary electrophoresis is presented. In this approach the sol-gel process is carried out inside 25 μm I.D. fused-silica capillaries. The sol solution contained appropriate quantities of an alkoxide-based sol-gel precursor, a polymeric coating material (Ucon), a crosslinking reagent, a surface derivatizing reagent, controlled amounts of water and a catalyst dissolved in a suitable solvent system. The coating procedure involves filling a capillary with the sol solution and allowing the sol-gel process to proceed for an optimum period. Hydrolysis of the alkoxide precursor and polycondensation of the hydrolyzed products with the surface silanol groups and the hydroxy-terminated Ucon molecules lead to the formation of a surface-bonded sol-gel coating on the inner walls of the capillary. The thickness of the coated film can be controlled by varying the reaction time, coating solution composition and experimental conditions. Commercial availability of high purity sol-gel precursors (e.g., TEOS 99.999%), the ease of coating, run-to-run and column-to-column reproducibility, and long column lifetimes make sol-gel coating chemistry very much suitable for being applied in analytical microseparations column technology. Test samples of basic proteins and nucleotides were used to evaluate the column performance. These results show that the sol-gel coating scheme has allowed for the generation of biocompatible surfaces characterized by high separation efficiencies in CE. For different types of solutes, the sol-gel coated Ucon column consistently provided migration time R.S.D. values of the order of 0.5%. The experimental section of Hayes is identical or equivalent to page 22, lines 8-24 of the instant specification. Also figure 1 of Hayes is identical to figure 3 of the instant specification. In the first paragraph of the paper Hayes discusses the problems associated with fused-silica capillary columns cause by the adsorption of biomolecules with acidic silanol groups on the inner surface of the capillary. The last full paragraph of the left column of page 4 teaches several advantages of the sol-gel technique including the strong adhesion of the coating due to the chemical bond

formed. The last paragraph of page 5 teaches the cleaning of the capillary followed by addition of the coating solution. The paragraph bridging the columns of page 6 discusses the factors that are responsible for the adsorption problem. Relative to the silanol groups Hayes teaches that a uniform distribution of the groups is necessary to achieve a uniform coverage of the chemically bonded organic coatings. The same paragraph teaches that untreated fused-silica capillaries are characterized by low concentrations and non-uniform distributions of these groups on the inner surface. This paragraph teaches that there is also the possibility for new silanol groups to be formed through reaction of the surface with atmospheric moisture. Consequently, chemical research into creation of silica surfaces with uniformly distributed silanol groups at their optimum concentration is fundamentally important for the overall development of column technology for capillary electrophoresis and other separation techniques. Important to the instant claims is the statement in this paragraph that a "silica surface with uniformly distributed silanol groups should be very much suited for its further chemical modification using various polymeric and monomeric reagents with functional groups that can react with silanol groups". Also in this paragraph is the statement that these "chemically bonded coatings will ensure effective coverage of the surface and reliably shield the residual silanol groups to prevent their participation in solute adsorption phenomena." Hayes does not teach a hydrothermal treatment.

In the paper Ogden discusses characterization of fused-silica capillary tubing by contact angle measurements. The capillary rise method was used to obtain angle measurements on untreated fused silica and fused silica treated with a variety of deactivating reagents. The contact angle data were used in the construction of Zisman plots which allowed characterization of the wettability of the surfaces by their critical surface energies. The wettability of raw fused silica was found to be widely variable which adversely affects attempts to fully deactivate the surface. **Hydrothermal** treatment of the fused silica with HNO_3 was found to be adequate for cleaning and hydroxylating the surface so as to allow complete deactivation. Simple silylating reagents, cyclic siloxanes, and polysiloxanes covering a wide range of polarity were used and evaluated as deactivating reagents. On page 8 the first four full paragraphs are relevant to the instant claims in that they teach that for fused-silica, columns coated with a stationary phase without deactivation of the fused-silica surface will often exhibit undesirable activity toward the analytes. Ways of deactivating the surface and enhancing the wettability have been the focus of much

research in capillary columns. The most satisfactory method of doing this is through chemical modification of the surface to replace the surface hydroxyl groups with silyl ether groups containing functional groups that are similar to or identical with those in the stationary phase. The paper looks at various hydrothermal and deactivation procedures and produces inert capillary gas chromatographic columns that have a high degree of surface coverage and are free of reversible and irreversible adsorption of nanogram levels of alcohols, amines and acids. The first two full paragraphs of page 14 compare the various procedures used to treat the columns including no treatment, rinsing and a hydrothermal treatment. Of note is the variability in the untreated columns and the incomplete deactivation of the columns when the columns are only rinsed compared to the completely deactivated surface when the columns are hydrothermally treated. This is again stated in the first full paragraph of page 16 in that the water and methanol rinses were not sufficient to remove whatever surface structure gave rise to the deactivation differences while the hydrothermal treatment was. The hydrothermal treatment was then characterized as "a necessary precaution to not only fully hydroxylate the surface but also to clean it."

In the paper Sumpter discusses static coating of 5 to 50 μm I.D. capillary columns for open tubular column chromatography. Dichlorofluoromethane, CCl3F, and Me4Si were used in the static coating of small diameter capillary columns (5 to 50 μm I.D.) to obtain highly efficient columns for gas and supercritical fluid chromatography. Capillary columns of 5-, 10-, 25-, and 50-μm I.D. were coated with stationary phase films of SE-33, SE-54, OV-215, 50% octyl, 45% phenoxypolyethyl ether, 50% liquid crystal, 25% biphenyl, 50% pentafluorophenyl, and 50% cyanopropyl polysiloxane stationary phases. Resultant evaluations of these columns in gas chromatography gave ~9000, 66000, 45000, and 19000 plates m^{-1}, respectively, for the different internal diameters. Important parameters affecting coating efficiency are identified and discussed in detail. Page 504 teaches that several preparation methods have been used for open tubular chromatography columns. Relative to the instant claims is the discussion of the chemical bonding method of coating the tubes. Page 506 teaches treating the columns prior to deactivation by a hydrothermal treatment and a dehydration treatment.

In the paper Hayes '96 highlights attractive features of sol-gel technology for the preparation of high performance columns for capillary chromatography and electrophoresis.

Aqueous and nonaqueous sol-gel chemistry based methodologies for the preparation of microcolumns for chromatography and capillary electrophoresis are presented. Both surface coated open tubular and in-situ packed capillary columns were prepared. The aqueous sol-gel was used for the in-situ packed columns while the nonaqueous sol-gel was used for the surface coated open tubular columns. Relevant to the instant claims, the last paragraph of page 497 teaches that they described a nonaqueous sol-gel method for the preparation of highly efficient open tubular columns for gas chromatography. The newly cited and applied Wang reference is the reference cited by Hayes '96. In the same paragraph they also state that this paper reports a nonaqueous sol-gel technique for the preparation of a highly efficient column for capillary electrophoresis. Page 498 shows that the preparation of the sol solution differs from that of the Hayes '97 preparation in that it is nonaqueous.

The Wang reference that was cited by Hayes '96 teaches the preparation of open tubular columns for capillary gas chromatography by a nonaqueous sol-gel method. On pages 506-507 the columns preparation of these columns uses a substantially similar composition to that taught in the Hayes '96 reference. The primary difference between the Wang sol-gel composition for capillary columns intended for gas chromatography when compared with the sol-gel composition for capillary electrophoresis columns is the use of polymethylhydrosiloxane in place of dicumyl peroxide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the hydrothermal treatment of Ogden or Sumpter into the method of Hayes because of the recognized problem in surface coverage during the deactivation step as discussed by Hayes, Ogden and Sumpter and the ability of the hydrothermal treatment to produce a reproducible fully hydroxylated surface as taught by Ogden and the expectation taught by Hayes that a silica surface with uniformly distributed silanol groups should be very much suited for its further chemical modification using various polymeric and monomeric reagents with functional groups that can react with silanol groups and these chemically bonded coatings will ensure effective coverage of the surface and reliably shield the residual silanol groups to prevent their participation in solute adsorption phenomena. Optionally it would have been obvious to one of ordinary skill in the art at the time the invention was made to change the composition of Hayes '97 based on the differences in the composition of the Hayes '96 and

Wang references because as shown by Wang and Hayes '96 a sol-gel coating composition for a column intended to be used for gas chromatography is substantially similar to one intended to be used for capillary electrophoresis and the benefits of using a sol-gel coating method for both types of columns as taught by Hayes '96, Hayes '97 and Wang.

6. The declaration under 37 CFR 1.132 filed June 13, 2005 is insufficient to overcome the rejection of claims 21-40 based upon either 35 USC 112 first paragraph or 35 USC 103(a) as set forth in the last Office action because of the following reasons. First, relative to the rejection under 35 USC 112 first paragraph, there are a number of ways that cross-linking can occur as noted above. Also it is noted that in the Hayes '97 reference, that scheme 3 shows the Ucon condensing with both the tetrahydroxysilane and the derivatized fused silica surface. Scheme 4 of Hayes '97 clearly shows that the "cross-linking" reaction increased the size of the polyalkylene glycol attaches to the sol gel derivatized surface but does not appear to join Ucon molecules on the derivatized surface. This does not appear to change the fact that the Ucon molecule is a polar molecule. Relative to the obviousness rejection examiner points out that the Ucon molecule is recognized as a polar molecule which would interact with and cause separation of molecules based on that property. Further more examiner points to the newly cited Wooley reference (US 5,192,406). In particular column 3, line 57 to column5, line 21 discuss a number of things. Particularly relevant to the instant declaration is the discussion related to capillary columns for gas chromatography and the discovery that surface deactivation methods that were previously used for gas chromatographic methods are applicable to columns used for capillary electrophoresis or capillary zone electrophoresis. This clearly connects the two types of columns contrary to what the declaration says. Thus, the declaration is not persuasive because 1) the Ucon material is a recognized polar material that would have been recognized by one of ordinary skill in the chromatographic art to have properties suitable for causing a separation between molecules based on that property; 2) the cross-linking shown by Hayes '97 would have been recognized by those of skill in the art as not destroying the polarity property of the Ucon material and ; 3) the newly cited Wooley reference shows a clear connection between capillary gas chromatography and capillary electrophoresis columns relative to deactivation of the column surface.

7. Applicant's arguments filed June 13, 2005 have been fully considered but they are not persuasive. Relative to the new matter rejection, examiner could find no basis in the instant specification as originally filed to specifically exclude a cross-linked organic ligand. The claims are to methods of preparing capillary columns and the specification does not teach that a cross-linked organic ligand would not function as a separate material for a gas chromatography process. Thus there is no basis for this type of limitation. If applicant wishes to use closed language to exclude elements of the composition of Hayes '97, that would find support in the original disclosure. For that reason, the claims have been treated in a manner that optionally shows the obviousness of removing the cross-linking agent when one is intending the composition for coating a column for gas chromatography. In this respect the applied Hayes '96 and Wang references clearly show that one of ordinary skill in the art would have changed the composition using a similar composition without the cross-linking agent found in Hayes '97. Additionally as shown above the declaration is not persuasive for the reasons given above and therefore does not support the arguments of applicant.

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The newly cited art is discussed above in relation to forming columns.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose at telephone number is (571) 272-1265. The examiner's schedule is variable between the hours of about 6:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

A general phone number for the organization to which this application is assigned is (571) 272-1700. The fax phone number to file official papers for this application or proceeding is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Arlen Soderquist

September 16, 2005

ARLEN SODERQUIST
PRIMARY EXAMINER